REMARKS

The Examiner has issued an Official Action in which it is stated that the claims in this application define eight different inventions. These are identified by the Examiner as:

Group I: Claims 1-9, drawn to a composition comprising 5-methoxytryptamine,

Group II: Claims 10-12 and 28, drawn to a method of preventing tissue damage,

Group III: Claims 13-15 and 29, drawn to a method of treating tissue damage,

Group IV: Claims 16-18, 21 and 24, drawn to a method of treating cardiac toxicity, myocardial ischemia, myocardial infarction or heart failure,

Group V: Claims 19-20 and 30, drawn to a method of increasing the activity of superoxide dismutase enzyme,

Group VI: Claims 22-23 and 31, drawn to a method of inhibiting lipid peroxidation,

Group VII: Claims 25-26, drawn to a method for reducing levels of creatine kinase-MB,

Group VIII: Claims 27 and 32, drawn to a method of reducing levels of lactate dehydrogenase.

This restriction requirement is respectfully traversed.

It is submitted that the claims as presented in this response all define a single invention and thus should all be examined in this application.

The subject matter of the present invention is the cardioprotective action of 5-

Methoxytryptamine or a pharmaceutically acceptable salt thereof and a pharmaceutical composition of the 5-Methoxytryptamine or the salt thereof for administration to a patient for obtaining such a cardioprotective action. Included in cardioprotective action is the protective action, the treatment and prevention of damage to cardiac tissue. This also includes treatment of cardiac toxicity, myocardial ischemia, myocardial infarction and heart failure.

As discussed in the specification, the heart, is susceptible to actions by chemotherapy drugs, which act as toxins and can cause damage to heart, which may develop into cardiac complications. Several chemotherapy drugs may cause cardiac toxicity. The chemotherapy drugs called anthracyclines are known to cause cardiac toxicity in patients. Anthracyclines such as doxorubicin, daunomycin, epirubicin, and idarubicin are frequently prescribed in various types of cancer treatments and are well known to cause damage to the muscle cells of the heart. The anthracyclines are also given with other drugs, such as alkylating agents and vinca alkaloids, which can contribute to heart damage. In addition, radiation therapy to the chest wall or area around the heart can affect the blood vessels supplying the heart, leading to a myocardial infarction or "heart attack". Since many patients, especially with lymphoma or breast cancer, receive both anthracycline-based chemotherapy and radiation therapy, there may be a cumulative effect on the heart. At present one way to prevent, limit or reduce cardiac complications from anthracyclines is to limit the amount of anthracyclines administered. However, this may not be a preferred way to treat a cancer patient.

Most of the cardiac complications associated with chemotherapy occur during or shortly after the completion of therapy. However, some of these problems can persist and become chronic.

In addition, some chemotherapy drugs can cause heart damage that is only apparent months to years after the completion of cancer treatment.

Further, normal tissues have a number of enzymatic scavenger mechanisms such as superoxide dismutase, catalase and the glutathione redox cycle. The myocardium has relatively low levels of these enzymatic scavenger mechanisms, and this is thought to contribute towards the vulnerability of myocardial tissue to anthracyclines. Moreover, there is also a nonenzymatic pathway of free radical production producing an anthracycline-iron complex that may further increase the risk of cardiotoxicity. Based on these elctrophysiological changes, there exists several enzyme markers as well as serum markers indicative of tissue injury/ischemia / stress/ or hypoxia. These include enzymes like creatinine kinase and its myocardium specific isoform i.e. creatinine kinase MB (CK-MB), lactate dehydrogenase, superoxide dismutase and membrane lipid peroxidation. The activity of these markers is a well-accepted index of cardiac toxicity. For example, e.g. CK-MB is a currently accepted serum marker in the World Health Organization (WHO) guidelines for the diagnosis of acute myocardial infarction and has become the "Gold Standard" for assessing myocardial infaraction. Further, anthracycline treatment produces significant elevation in CK-MB levels in cardiac tissues.

Therefore, an agent, which would

1) reduce the elevated CK-MB levels in tissues;

2) reduce the elevated levels of lactate dehydrogenase in tissues;

3) increase the activity of superoxide dismutase enzyme in tissues; or

4) inhibit lipid peroxidation in a tissue

can be utilized as a cardioprotective agent. Such cardioptective agents may act either through any such single mechanism or may have a combination of the abovementioned effects. The present applicants have found that 5-methoxy tryptamine reduces the CK-MB, lactate dehydrogenase levels in tissues, also inhibits lipid peroxidation and also causes an increase in the activity of superoxide dismutase enzyme and therefore can be utilized in prevention and treatment of cardiac toxicity. Further, the pre-clinical experiments included in the present specification provide evidence that the 5-methoxy tryptamine is a potent cardioprotective agent acting through various abovementioned pathways.

Thus, claims 10 to 27 and 32 to 43 are related to a single action i.e. a cardioprotective effect, as described above, of 5-methoxy tryptamine. Claims 10-12 and 28 are directed towards prevention of cardiotoxicity or protection of cardiac tissue and claims 13-15 and 29 are drawn towards treatment of cardiotoxicity whereas claims 16-18, 21 and 24 are drawn towards a method of treating such cardiotoxicity. Claims 19-20 and 30 claim a cardioprotective effect through increase in superoxide dismutase activity; claims 22-23 and 31 claim a cardioprotective effect through inhibition of lipid peroxidation; claims 25-26 and 42 claim a cardioprotective effect through reducing elevated levels of CK-MB in tissue and claims 27, 32 and 43 claim a cardioprotective effect through reducing elevated levels of lactate dehydrogenase. All of the claims are related to single action i.e. a cardio protective effect of 5-methoxy tryptamine and therefore, restriction to one particular mechanism of action for elucidating a cardioprotective response by selecting any particular set of claims, would result in a limited protection and therefore, reconsideration of restriction action is sought.

It is known in the pharmaceutical arts that most pharmaceutically active compounds or salts are administered in some form of pharmaceutical composition. Example of pharmaceutical compositions include and are not limited to tablets, capsules, powders, lozenges, solutions, syrups, aqueous or oily suspensions, elixirs, implants, and aqueous or non-aqueous injections. Thus claims drawn towards the pharmaceutical composition i.e. claims 1-9 (group I) is an integral part of the present invention and must be examined with the method claims.

In view of the above, the present applicants strongly feel that the restriction requirement is unwarranted and that all of the claims define a single invention and should be examined in the same application.

If the examiner disagrees with applicants' assessment and does not withdraw or reformulate the restriction requirement, applicants' provisionally elect the claims of Group IV-Claims 16-18, 21 and 24. In addition, in view of the amendment of the claims, it is respectfully requested that at least claims 39-43 also be examined with the claims of Group IV.

All rights to file one or more divisional applications directed to any subject matter disclosed in the specification, claimed at the time of filing this application or presently claimed is preserved.

Applicants submit that the present application is in condition for allowance and favorable consideration is respectfully requested.

Respectfully submitted,

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